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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,356	02/05/2004	Leslie P. Weiner	23714-07992	6800

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/773,356	WEINER ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/8/08, 6/9/08, 6/19/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9,12,14-19,23,26,28 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9,12,14-19,23,26,28 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/19/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 6/09/08 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and remarks filed 5/08/08, and IDS filed 6/19/08 have been entered.

2. Claims 8, 9, 12, 14-19, 23, 26, 28, and 30 are pending and under examination.

3. In view of Applicant's amendment, the previous rejection of Claim 30 under the first paragraph of 35 U.S.C. 112 for the introduction of new matter into the claims has been withdrawn. Additionally, given the additional limitations that have been added to Claim 30, the previous rejection under 35 U.S.C. 103(a) has also been withdrawn. In particular the combined references do not teach a method comprising the administering of PBMCs.

4. Claim 30 is objected to; Il-2 would properly be IL-2.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 8, 9, 12, 14-19, 23, 26, and 28 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) … T cells are cultured in the presence of whole bovine myelin proteins or synthetic human proteins … attenuated T-cell lines … (Claim 8).

Applicant cites page 7-12 of the specification for support.

At page 8 the specification discloses PBMCs are cultured in the presence of cow myelin proteins or synthetic complete human proteins. A review of the cites does not reveal T cells prepared by the claimed method. The specification discloses the culturing of PBMCs and not just T cells. Regarding T-cell lines, a review of the cites reveals that T cell lines are disclosed only at page 12. Said disclosure is then only in the context of Example 1 and thus appropriate only for the method of Claim 30.

Applicant's arguments, filed 5/08/08 have been fully considered but they are not persuasive. Applicant again cites pages 7-12, additionally cites the original claims, and argues that what is well known need not be disclosed. Regarding the T cell lines of the claim, Applicant argues that T-cell lines are actually polyclonal T cells.

Again, the specific limitations of the claims have not been found anywhere in the specification. While the specification may disclose vaccines comprising T cells, the method of making the vaccine comprising T cells recited in the claims employs PBMCs. A review of the original claims shows that Claims 8-19 are drawn to a method of mediating an immune response, but they do not recite a method employing a vaccine comprising T cells cultured in the presence of whole bovine myelin proteins. Regarding the argument that what is well known need not be disclosed, specific method steps not found in the specification will be considered to comprise new matter.

Regarding Applicant's now defining of T-cell lines as polyclonal T cells, such would not be the customary and accepted definition of the term. Cell "lines" are more routinely defined as clones (see, for example encarta.msn.com or pbs.org) or transformed cells (see, for example, biology-online.org or cancerweb.ncl.ac.uk).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 8, 9, 12, 14-19, 23, 26, and 28 stand rejected under 35 U.S.C. 103(a) each as being unpatentable over Stinissen et al. (1996) in view of Correale et al (1995) and the background teachings of the specification.

As set forth previously, Stinissen et al. teaches a method of mediating an immune response comprising administering subcutaneously irradiation-attenuated T-cells derived from autologous peripheral mononuclear cells (comprising T cells) cultured in the presence of natural or synthetic human myelin proteins (see particularly page 503, T CELL VACCINATION IN MS).

The reference differs from the claimed invention only in that it does not teach the use of attenuated T cells that target more than one myelin protein and in that it does not teach the optimization of the claimed method as set forth in dependent Claims 16-19.

Correale et al. extends the teachings of Stinissen et al. regarding additional MS autoantigens. The reference teaches that as MS develops, myelin breakdown exposes additional myelin antigens (besides MBP) to autoreactive T cells, thus, broadening the autoimmune response (see particularly page 1375, last paragraph - page 1376, first paragraph. The reference further teaches the use of bovine brain as a source of myelin proteins (see particularly page 1371, column 2).

The background (Description of the Related Art) section of the specification further supports the teachings of Correale et al. See, for example, page 2 wherein the specification discloses "Presently, the myelin proteins thought to be the target of an immune response in MS include myelin basic protein (MBP), proteolipid protein (PLP), myelin associated glycoprotein (MAG), and myelin-oligodendrocyte glycoprotein (MOG). Also there is an increasing body of evidence that the T-cell receptor has extraordinary flexibility, allowing it to react to many different proteins (Brock R., K.H. Wiesmuller, et al. (1996) Proc. Natl. Acad. Sci. (USA) 93:13108-13113; Loftus D.J., Y. Chen, et al. (1997) J. lmmunol. 158:3651-3658)." The specification additionally discloses, "In both EAE and MS, myelin basic protein (MBP), proteolipid protein (PLP), and MOG are thought to be the main target antigens for autoreactive T-cells (Brostoff S.W. and D.W. Mason (1984) J. Immunol. 133:1938-1942; Tabira and Kira, 1992). Myelin associated glycoprotein (MAG) may be important in MS but does not produce EAE in experimental models."

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform the method of administering attenuated T cells, as taught by Stinissen et al., employing attenuated T cells autoreactive to multiple human myelin antigens. One of ordinary skill in the art at the time the invention was made would have been motivated to employ attenuated T cells autoreactive to multiple myelin antigens given the teachings of Stinissen et al. that MBP is not the only autoantigen candidate in MS, extended by Correale et al. that as MS develops, myelin breakdown exposes additional myelin antigens (besides MBP) to autoreactive T cells, thus broadening the autoimmune response, and the background teachings of the specification that multiple protein antigens are targeted in MS. One of ordinary skill in the art at the time the invention was made would also have been motivated to employ myelin proteins obtained from bovine as a convenient source of said proteins given the teachings of Correale et al. of the availability of said source. Further, the choice of dosage (Claim 17), and timing (Claim 16), would

have fallen well within the purview of the skilled artisan at the time of the invention. Regarding the increasing of the dosages as set forth in Claims 18 and 19, one of ordinary skill in the art at the time the invention was made would have been well aware of the concept of increasing dosage if no response is obtained up to the point of efficacy or adverse reaction. These limitations do not render the claimed method patentably distinct.

Applicant's arguments filed 5/08/08 have been fully considered but they are not persuasive. Applicant argues that the claimed invention does not encompass the administration of isolated T cell clones.

A review of independent Claim 8 shows it to recite "administering attenuated T-cell lines to a human". As set forth previously, "T-cell lines" encompass the clones of the references.

Applicant argues a lack of expectation of success.

Whether the T cells used in vaccination were isolated from blood or CSF before expansion is irrelevant. Sufficient T cells were isolated and expanded such that vaccination could be performed. The claimed method comprises a method of treating MS, not a method of producing a T cell vaccine. It is enough that the combined references demonstrate that a T cell vaccine could be made and that it was administered to a human.

9. The following are new grounds for rejection.

10. Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, A method of administering attenuated PBMCs.

Applicant cites original Example 1 (page 10) of the specification in support.

A review of the cite reveals the administration of myelin specific T cells separated from APCs (and other PBMCs) by Ficoll™ gradient (page 11).

11. No Claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara, Ph.D. can be reached on (571) 272-0878.

13. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

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